PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 33/MG	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/GB2004/001008	International filing date *(day/month/year)* 10.03.2004	Priority date *(day/month/year)* 14.03.2003
International Patent Classification (IPC) or national classification and IPC C07D487/04, C07D519/00, A61K31/5025, A61P3/10, A61P17/06, A61P19/02, A61P37/00		
Applicant AVIDEX LIMITED et al.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 6 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
13.10.2004	14.03.2005
Name and mailing address of the international preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer Bosma, P Telephone No. +31 70 340-3665

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/GB2004/001008

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:

   ☐ international search (under Rules 12.3 and 23.1(b))
   ☐ publication of the international application (under Rule 12.4)
   ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

   Description, Pages

   1-66 as originally filed

   Claims, Numbers

   1-29 as originally filed

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:

   ☐ the description, pages
   ☐ the claims, Nos.
   ☐ the drawings, sheets/figs
   ☐ the sequence listing *(specify)*:
   ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

   ☐ the description, pages
   ☐ the claims, Nos.
   ☐ the drawings, sheets/figs
   ☐ the sequence listing *(specify)*:
   ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 27-29

because:

☒ the said international application, or the said claims Nos. 27-29 with respect to IA relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-29
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-29
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-26
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 27-29 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

For the assessment of the present claims 27-29 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1: WO 03/004495 A (SOERENSEN POUL ; DA GRACA THRIGE DORTHE (DK); ACTIVE BIOTECH AB (SE);) 16 January 2003 (2003-01-16)

D2: US-A-4591589 (HUMBERT DANIEL ET AL); 27 MAY 1986

D1 describes N-phenyl substituted 3-oxo-dihydropyrazolo[4,3-c]**quinolin-2-yl** derivatives as CD80 antagonists (immunomodulating compounds), from which the compounds of the present application mainly differ in being **specific R_4-X**-substituted 2-phenyl-3-oxo-dihydropyrazolo[4,3-c]**cinnolin-2-yl** derivatives having the same use as CD80 antagonists (immunomodulating compounds).

D2 discloses 2-aryl-pyrazolo[4,3-c]cinnolin-3-ones having anxiolytic properties, in which the aryl group is optionally substituted by alkyl, alkoxy, halogen, halomethyl or aralkoxy, and being different from the present specific R_4-X-substituents.

Therefore the present application satisfies the criterion set forth in Article 33(2) PCT and is considered to be new in respect of the prior art as defined in the regulations

(Rule 64(1)-(3) PCT).

The problem to be solved by the present application is to provide further compounds, which are useful as CD80 antagonists (immunomodulating compounds). This problem has been solved by the specific R_4-X-substituted 2-phenyl-3-oxo-dihydropyrazolo[4,3-c]**cinnolin-2-yl** derivatives of formula (I) of the present application. From the available prior art there were no incentives to use the above mentioned 2-phenyl-3-oxo-dihydropyrazolo[4,3-c]**cinnolin-2-yl** derivatives for the indicated pharmaceutical use. The present application consequently satisfies the criterion set forth in Article 33(3) PCT, because the subject-matter of claims 1-29 is considered to be not obvious and to involve an inventive step in respect of Rule 65(1)(2) PCT.

With respect to the industrial applicability of claims 27-29 see Section III above.

2) Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D1 and D2 is not mentioned in the description, nor are these documents identified therein.

3) "**Optionally substituted**", as used in the present claims 1,9,11, and 13, has the meaning "substituted by absolutely anything". However such a broad term is objected to under Article 33(3) PCT, because it is very unlikely that substantially all compounds covered by these broad claims are useful as androgen receptor antagonist. Therefore these claims relate to subject-matter which is not inventive.

4) Claim 19 comprises all the features of claim 1 and is therefore not appropriately formulated as a claim dependent on the latter (Rule 6.4 PCT).

5) Claims 22 and 23 comprise all the features of claim 1 and are therefore not appropriately formulated as claim dependent on the latter (Rule 6.4 PCT).

6) The applicant is requested to file amendments by way of replacement pages in the manner stipulated by Rule 66.8(a) PCT. In particular, fair copies of the amendments should be filed preferably in triplicate.
Moreover, the applicant's attention is drawn to the fact that, as a consequence of Rule 66.8(a) PCT the examiner is not permitted to carry out any amendments under the PCT procedure, however minor these may be.